Defining high-risk patients for endovascular aneurysm repair

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Background: **Endovascular aneurysm repair (EVAR) is commonly used as a minimally invasive technique for repairing infrarenal aortic aneurysms. There have been recent concerns that a subset of high-risk patients experience unfavorable outcomes with this intervention. To determine whether such a high-risk cohort exists and to identify the characteristics of these patients, we analyzed the outcomes of Medicare patients treated with EVAR from 2000-2006.**

Methods: **We identified 66,943 patients who underwent EVAR from Inpatient Medicare database. The overall 30-day mortality was 1.6%. A risk model for perioperative mortality was developed by randomly selecting 44,630 patients; the other one third of the dataset was used to validate the model. The model was deemed reliable (Hosmer-Lemeshow statistics were $P = .25$ for the development, $P = .24$ for the validation model) and accurate (c = 0.735 and c = 0.731 for the development and the validation model, respectively).**

Results: **In our scoring system, where scores ranged between 1 and 7, the following were identified as significant baseline factors that predict mortality: renal failure with dialysis (score = 7); renal failure without dialysis (score = 3); clinically significant lower extremity ischemia (score = 5); patient age ≥85 years (score = 3), 75-84 years (score = 2), 70-74 years (score = 1); heart failure (score = 3); chronic liver disease (score = 3); female gender (score = 2); neurological disorders (score = 2); chronic pulmonary disease (score = 2); surgeon experience in EVAR <3 procedures (score = 1); and hospital annual volume in EVAR <7 procedures (score = 1). The majority of Medicare patients who were treated (96.6%, n = 64,651) had a score of 9 or less, which correlated with a mortality <5%. Only 3.4% of patients had a mortality ≥5% and 0.8% of patients (n = 509) had a score of 13 or higher, which correlated with a mortality >10%.**

Conclusion: **We conclude that there is a high-risk cohort of patients that should not be treated with EVAR because of prohibitively high mortality; however, this cohort is small. Our scoring system, which is based on patient and institutional factors, provides criteria that can be easily used by clinicians to quantify perioperative risk for EVAR candidates. (J Vasc Surg 2009;50:1271-9.)**

With a greater awareness through the liberal use of cross-sectional imaging and enhanced screening efforts, abdominal aortic aneurysms (AAA) are being identified with increasing frequency.[1,2] With multiple comorbidities that are associated with an increased risk of intervention, this population presents a unique challenge to vascular interventionalists. Endovascular repair of AAA (EVAR) was first introduced in 1991 by Parodi et al.[3] Fifteen years later, it appears that EVAR will soon become the predominant method of AAA repair.[4] Because it is minimally invasive, EVAR potentially holds great advantage for high-risk patients with multiple comorbidities. The procedure does not require general anesthesia or intensive care unit (ICU) admission postoperatively. Additionally, EVAR requires only femoral artery exposure, eliminating the need for a laparotomy and its complications. There is decreased blood loss compared with open repair, and the major perioperative intravenous fluid shifts observed with open repair are avoided. It has been previously demonstrated that the perioperative morbidity and mortality associated with endovascular repair approaches one fourth that of traditional open surgery.[4]

These advantages suggest that a broad spectrum of AAA patients should be appropriate candidates for the endovascular approach. However, the concept that EVAR is applicable to all patients regardless of the severity of their comorbidities has recently been challenged. In the EVAR 2 trial,[5] Greenlaugh and coauthors identified a cohort of patients "unfit for open repair" and randomized these patients to EVAR versus medical treatment. These investigators found that there was no significant difference in all-cause mortality between medical treatment and EVAR, with EVAR patients having a perioperative mortality of 9%. These authors concluded that for high-risk AAA patients, no surgical intervention is warranted. Despite valuable insights from EVAR 2, there are unanswered questions: how large is the subset of patients who are high risk for EVAR

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and what are the preoperative characteristics that can identify them?

Several studies have reported risk stratification paradigms for open AAA repair.[6-10] Subgroups of patients, who are at high or even prohibitively high risk for conventional AAA repair, have been identified. Variables that have been commonly defined as pre-operative risk factors for mortality include: increased age, congestive heart failure (CHF), myocardial ischemia, and renal and pulmonary dysfunction.[6,7,9,11] By comparison, such risk factors have not been identified for patients undergoing EVAR. Specification of these risk factors is essential to delineate those patients at prohibitive risk for EVAR who would benefit from medical therapy alone. Thus, to better understand the mortality associated with EVAR and, more importantly, to define patients at excessively high risk for this "minimally invasive" procedure, we analyzed the outcomes of Medicare patients treated with EVAR between 2000 and 2006.

MATERIALS AND METHODS

Data sources and study population. We used the Medicare Inpatient Standard Analytical file (Medicare part A) to identify hospitalized patients who underwent EVAR between 2000 and 2006. These files contain hospital-discharge abstracts on 100% of Medicare-reimbursed hospitalizations, except for those beneficiaries enrolled in Medicare HMOs (approximately 10% of patients). The data were supplemented with the Medicare Denominator file, which contains demographic, geographic, and vital status data. The data were obtained from the Centers for Medicare and Medicaid Services (CMS).

Patients who underwent AAA repair were identified through a combination of the International Classification of Diseases, Clinical Modification (ICD-9-CM) diagnosis code, 441.4 (aortic abdominal aneurysm without mention of rupture) in the primary or any secondary position, plus the primary or any secondary ICD-9-CM procedure code, 39.71 (endovascular implantation of graft in abdominal aorta). If a patient had multiple AAA repairs, the first AAA procedure was included in the analysis. Only patients with elective admissions were included in this study. To ensure that all comorbidities identified at prior hospitalizations were not missed, we used a longer time period (1995-2006) to define the comorbidities of patients who were ultimately treated with EVAR.

It is often difficult to differentiate between pre-existing comorbidities and postoperative complications (eg, stroke) in large datasets. To address this weakness, we included a diagnosis as a comorbidity if 1) it was present on a previous hospital admission or 2) if it appeared during the index hospitalization and was coded as a chronic or "acute on chronic" disorder. The following comorbidities were assessed (primary and all secondary diagnoses): cardiac disease (coronary artery disease, congestive heart failure [CHF], valvular heart disease, cardiac arrhythmias), diabetes, chronic pulmonary disease, peripheral arterial disease (clinically significant lower extremity ischemia, vascular insufficiency of the intestine, and renal atherosclerosis), renal disease, neurological disorders (cerebrovascular, paralysis, and other neurological diseases), cancer, rheumatoid arthritis, and liver disease. The list of ICD-9 diagnosis codes for comorbidities is provided in the Appendix (online only). The annual hospital volume (number of EVAR/year) and cumulative physician experience with EVAR at the time of the procedure were used to develop a relationship between EVAR volume/experience and outcome. All endovascular repairs (elective and ruptured) were included in calculations of hospital volume and surgeon experience.

Statistical analysis. To construct a risk model for perioperative mortality after EVAR, all patients were randomly allocated to a dataset for model development (the training set; n = 44,630, 2/3 of cohort) and a dataset for model validation (the test set; n = 22,313, 1/3 of the cohort). In deriving the model, we first analyzed the univariate associations between the independent variables (patient demographics, baseline comorbidities, hospital volume, and surgeon EVAR experience) and 30-day mortality. Continuous variables (age, hospital volume, and surgeon experience) were transformed into categorical variables. Hospitals annual volume and surgeon experience were categorized into 10 groups (deciles) with approximately equal distribution of patients between groups. Patients less than 65 years of age were excluded from the analysis to avoid some confounding issues due to their disability as a criterion for Medicare eligibility. Five-year increments were used for age groupings. A Chi-square test was used to assess the association between potential risk factors and mortality. Variables with a level of significance (P value) $< .25$ were included in a logistic regression analysis. This multivariable regression model examines dichotomous outcomes (dead/alive), and their associated risk factors. Only variables with P value $\leq .05$ were included in the final model. The interpretation of a risk factor included in the final model is that it is independently associated with the event, controlling for other significant covariates, and all risk factors jointly predict the event. Interactions between significant predictors and age, gender, and race/ethnicity were also tested. The diagnostic properties of the training model were then tested using the validation dataset. The area under the receiver operator curve (c statistic) was calculated as a measure of discrimination or predictive ability. A value of 1 indicates perfect discrimination. Calibration of the model (statistical precision) was assessed by the Hosmer-Lemeshow goodness-of-fit statistic. This statistic compares observed number of patients with expected, derived by logistic model. A P value for goodness of fit greater than 0.05 indicates that there is no statistical difference between observed and expected numbers and that the model has a high predictive ability. Risk factors were derived from the training model and verified on validation dataset.

The regression coefficients of the risk factors were used to develop a scoring system to predict 30-day mortality after EVAR. Regression coefficients were multiplied by a scaling factor and then rounded to the nearest integer.[12] The total risk score of a patient was the sum of the scores for

Table I. Patient demographics and 30-day mortality by demographic groups (n = 66,943 patients)

Variable	*No. of patients*	*% of cohort*	*Mortality (%)*	P *value*
Age, years				
65-69	12,046	17.99	0.9	(reference group)
70-74	16,994	25.39	1.2	0.04
75-79	18,624	27.82	1.6	<0.0001
80-84	13,311	19.88	2.0	<0.0001
≥85	5,968	8.92	3.2	<0.0001
Male	55,485	82.88	1.4	(reference group)
Female	11,458	17.12	2.5	<0.0001
Whites	63,492	94.84	1.6	(reference group)
Blacks	1,847	2.76	1.9	0.29
Hispanics	354	0.53	2.0	0.55
Native Americans	118	0.17	1.7	0.92
Other races	830	1.24	0.7	0.05

Table II. Comorbidities and their association with 30-day mortality (N = 66,943 patients)

Comorbidity	*No. of patients*	*% of cohort*	*Mortality (%)*	P *value*	*Odds ratio*
Renal failure w/dialysis	718	1.07	11.8	<.0001	9.01 [7.12-11.39]
Renal failure w/o dialysis	2,554	3.82	3.8	<.0001	2.64 [2.13-3.26]
PAD	4,855	7.25	3.1	<.0001	2.17 [1.82-2.58]
LE ischemia	1,414	2.11	6.2	<.0001	4.42 [3.52-5.53]
Vascular intestine	141	0.21	2.8	0.23	1.82 [0.67-4.93]
Renal atherosclerosis	3,409	5.09	1.9	0.09	1.24 [0.97-1.60]
Heart failure	9,644	14.41	3.5	<.0001	2.88 [2.53-3.28]
Neurological disorders	7,494	11.19	2.4	<.0001	1.63 [1.39-1.92]
Cerebrovascular and/or paralysis	5,282	7.89	2.1	0.0016	1.38 [1.13-1.68]
Other neurological	2,596	3.88	3.3	<.0001	2.23 [1.79-2.80]
Liver disease	728	1.09	3.2	0.0006	2.05 [1.35-3.13]
Cardiac arrhythmia	16,840	25.16	2.3	<.0001	1.78 [1.57-2.01]
Rheumatoid arthritis	1,311	1.96	2.3	0.04	1.47 [1.02-2.12]
Valvular disease	6,364	9.51	2.2	<.0001	1.44 [1.20-1.72]
Chronic pulmonary	24,854	37.13	2.0	<.0001	1.49 [1.32-1.68]
Atherosclerosis	5,378	8.03	1.7	0.49	1.08 [0.87-1.34]
Cancer	5,135	7.67	1.7	0.57	1.07 [0.85-1.33]
Diabetes	11,013	16.45	1.6	0.80	0.98 [0.83-1.15]
Coronary disease	36,664	54.77	1.5	0.03	0.88 [0.78-0.99]

LE, Lower extremity; *PAD,* Peripheral arterial disease.

each individual risk factor. Additional logistic regression model was constructed to evaluate the relationship between total risk score and mortality. The model was created using training dataset and was validated on test dataset. The 30-day mortality associated with total risk score was the average risk among all patients having the same total score. The accuracy of our scoring system was tested by comparing the predicted mortality associated with each risk score with the observed mortality on the validation dataset. All statistical analyses were performed using the SAS system software version 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

Risk factors: univariate analysis. We identified 66,943 patients age 65 or older who underwent EVAR between 2000 and 2006. Since Medicare dataset provides date of surgery, we were able to identify conversion cases. We excluded 48 patients who had an open AAA repair prior to an EVAR procedure during the same hospitalization. However, we retained all conversions from EVAR to open repair in the dataset. In terms of demographics, 8.9% of the study population was 85 years of age or older, 82.9% were males, and 94.8% were Caucasians (Table I). The overall 30-day mortality was 1.6%. The 30-day mortality after EVAR among females was higher than among males (2.5% vs. 1.4%; $P < .0001$). Perioperative mortality also increased with patient age; this became statistically significant for patients 70 years of age or older (Table I).

A number of baseline comorbidities were associated with 30-day mortality as shown in Table II. Common risk factors included chronic pulmonary diseases (37.1% of cohort, mortality 2.0%, $P < .0001$), cardiac arrhythmia (25.2%, mortality 2.3%, $P < .0001$), and heart failure

Table III. Annual hospital volume and cumulative surgeon experience over the study period and their association with 30-day mortality (n = 66,943 patients)

Variable	*No. of patients*	*% of cohort*	*Mortality (%)*	P *value*
Hospital EVAR Volume (Annual, deciles)				
1-6	7,924	11.84	2.3	.0001
7-10	7,011	10.47	1.6	.33
11-14	6,649	9.93	1.8	.06
15-18	5,940	8.87	1.5	.85
19-23	6,571	9.82	1.4	.91
24-30	6,790	10.14	1.6	.39
31-37	6,126	9.15	1.4	.86
38-49	6,789	10.14	1.2	.34
50-73	6,469	9.66	1.5	.83
74+	6,674	9.97	1.4	reference
Surgeon's EVAR experience (cumulative, deciles)				
1-2	7,895	11.79	2.4	<.0001
3-5	7,539	11.26	1.6	.16
6-8	5,844	8.73	1.8	.02
9-12	6,168	9.21	1.5	.36
13-18	6,957	10.39	1.5	.37
19-25	6,104	9.11	1.5	.36
26-36	6,597	9.85	1.5	.26
37-54	6,728	10.05	1.4	.63
55-93	6,504	9.72	1.4	.48
94+	6,607	9.87	1.3	reference

EVAR, Endovascular aneurysm repair.

(14.4%, mortality 3.5%, $P < .0001$). Patients with renal failure with dialysis represented only 1.1% of the cohort; however, their risk of dying after EVAR was highest (11.8%, $P < .0001$). Another less common risk factor strongly associated with mortality, was clinically significant lower extremity ischemia (2.1% of cohort, mortality 6.2%, $P < .0001$).

Finally, we evaluated the relationship between hospital annual volume and surgeon cumulative experience with EVAR and perioperative mortality (Table III). Mortality declined from 2.3% to 1.4%, with growing hospital annual volume from less than seven procedures versus volume greater than 73 EVARs (Table III). Thirty-day mortality, when EVAR was performed by surgeons with total experience of ≤ 2 procedures, was 2.4%, whereas the mortality was in the range of 1.3% to 1.6% for surgeons with a cumulative EVAR experience ≥ 3 procedures.

Multivariable model. In a multivariable regression model, the following baseline comorbidities predicted 30-day mortality after EVAR: renal failure with dialysis (odds ratio [OR] = 7.06, $P < .0001$) and without dialysis (OR = 1.91, $P < .0001$), clinically significant lower extremity ischemia (OR = 3.55, $P < .0001$), liver disease (OR = 2.52, $P < .0001$), CHF (OR = 2.23, $P < .0001$), neurological disorders (OR = 1.59, $P < .0001$), and chronic pulmonary diseases (OR = 1.57, $P < .0001$) (Table IV). The risk of death after EVAR was 68% higher for females versus males (OR = 1.68, $P < .0001$) and increases with patient age: OR = 1.40 for patients 75-79 years of age to OR = 3.10 for patients ≥85 years of age, controlling for comorbidities, gender, hospital volume, and surgeons experience. Hospital volume (< 7 EVARs per year) remained in the model as a predictor of death after surgery, as did surgeon experience of < 3 EVAR procedures at the time of the index operation.

Using the receiver operating curve characteristics, we found that the c-indices were 0.735 for the training set and 0.731 for the test set, indicating the robust predictive

Table IV. Statistically significant predictors of 30-day mortality after EVAR AAA (based on the results of multivariable logistic regression model, concordance index = 0.735, Hosmer-Lemeshow goodness of fit test $P = .25$)

Risk factor	*Parameter*	*Odds ratio and 95% CL*	P *value*
Renal failure w/ dialysis	1.95	7.06 [5.23-9.53]	<.0001
LE ischemia	1.27	3.55 [2.65-4.75]	<.0001
Age ≥ 85 years	1.13	3.10 [1.57-2.37]	<.0001
Liver disease	0.93	2.52 [1.54-4.12]	.0002
CHF	0.80	2.23 [1.89-2.64]	<.0001
Renal failure w/o dialysis	0.65	1.91 [1.45-2.51]	<.0001
Age 80-84 years	0.65	1.92 [1.56-2.36]	<.0001
Female	0.52	1.68 [1.42-1.99]	<.0001
Neurological	0.45	1.59 [1.29-1.94]	.0001
Chronic pulmonary	0.45	1.57 [1.35-1.83]	<.0001
Hospital annual vol <7	0.37	1.45 [1.18-1.80]	.0005
Age 75-79 years	0.34	1.40 [1.14-1.71]	0.001
Surgeon EVAR vol <3	0.26	1.30 [1.04-1.62]	.002

CHF, Congestive heart failure; *EVAR,* endovascular aneurysm repair; *LE,* lower extremity.

Table V. Risk scores for 30-day mortality for EVAR patients

Risk factor	*Score*
Renal failure w/dialysis	7
LE ischemia	5
Age ≥ 85 years	4
Liver disease	3
CHF	3
Renal failure w/o dialysis	3
Age 80-84 years	2
Female	2
Neurological	2
Chronic pulmonary	1
Surgeon EVAR experience <3	1
Hospital annual volume <7	1
Age 75-79 years	1

CHF, Congestive heart failure; *EVAR,* endovascular aneurysm repair; *LE,* lower extremity.

Table VI. Predicted mortality based on scoring system

Total risk score	*Predicted 30-day mortality (%)*	*No. of patients*
0	0.5	9907
1	0.7	7516
2	0.9	12005
3	1.1	9281
4	1.4	7656
5	1.7	6532
6	2.2	4715
7	2.8	3403
8	3.5	2274
9	4.4	1462
10	5.5	892
11	6.8	543
12	8.5	348
13	10.6	213
14	13.0	99
15	15.6	87
16	19.4	46
17	23.4	35
18	27.9	7
19	32.9	7
20	38.4	8

ability of these models. The Hosmer-Lemeshow goodness of fit statistics (comparison of observed and expected deaths) were 0.25 and 0.24 for training and test datasets respectively, indicating good statistical precision of the models.

Risk score. Table V depicts risk scores for every statistically significant risk factor. Risk scores ranged from a minimum of one point for chronic pulmonary disorders to a maximum of seven points for renal failure with dialysis. The total risk score was obtained by summing individual risk points. The regression model that evaluated the relationship between total risk score and 30-day mortality was deemed reliable (Hosmer-Lemeshow statistics was $P = .06$ for the development, $P = .83$ for the validation model) and accurate (c = 0.73 and c = 0.70 for the development and the validation model, respectively).

The relationship between predicted 30-day mortality after EVAR and patients' total risk score is presented in Table VI. The estimated mortality ranged from 0.5% to 38.4% for risk scores that ranged from 0 to 20. We then evaluated the agreement between predicted and observed mortality by risk score (Fig 1). The correlation between observed mortality (test dataset) and expected mortality (training dataset) using this model was very strong; $r^2 = 0.83$ ($P < .0001$).

The distribution of patients by risk score is shown in Fig 2: 96.6% (n = 64,651) of patients had a score of nine or less, which correlated with a mortality of less than 5%; 3.4% of patients (n = 2,292) had a score >9 and a mortality greater than 5%. Only 0.8% of patients (n = 509) had a score of 13 or higher, which correlated with a mortality of greater than 10%.

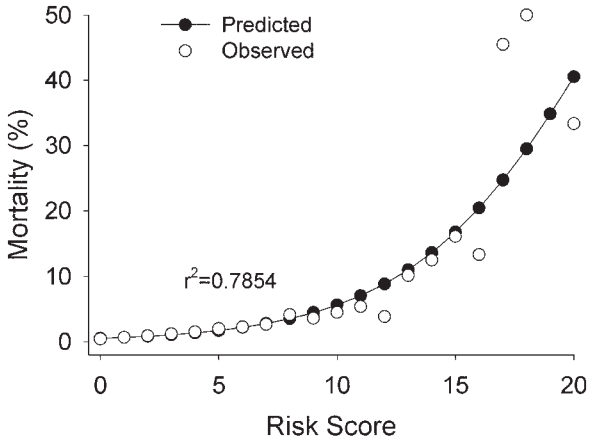

Fig 1. Relationship between observed and predicted mortality by total score. Predicted mortality was estimated based on logistic regression model of two thirds of the cohort (development sample). Observed mortality was depicted from the remaining one third of the cohort (test sample). Coefficient of correlation between observed and predicted mortality $r^2 = 0.8294$. Number of observations in the test sample by score: 1 – 3229, 2 – 2497, 3 – 4051, 4 – 2573, 5 – 2135, 6 – 1555, 7 – 1104, 8 – 800, 9 – 475, 10 – 312, 11 – 186, 12 – 130, 13 – 69, 14 – 24, 15 – 31, 16 – 15, 17 – 11, 18 – 2, 19 – 0, 20 – 3.

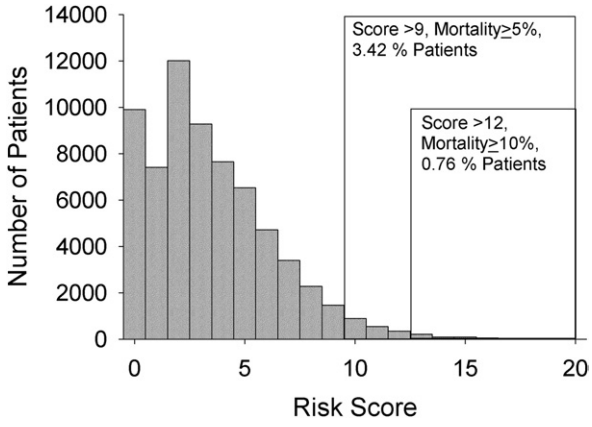

Fig 2. Distribution of patients by risk scores.

DISCUSSION

Numerous studies have compared the outcomes of open repair with EVAR, and the benefits of EVAR in terms of more intermediate outcomes have been well documented.[6,13-20] However, concerns have arisen as to whether EVAR is a sufficiently low-risk procedure that it can be used safely in all patients with AAA >5.5 cm. Greenlaugh and colleagues addressed this question with the EVAR trial 2. They identified a perioperative mortality of 9% in a population of patients with large aneurysms "unfit" for open surgery repaired with endovascular techniques.[5] These authors were the first to recognize and report the limitations of EVAR and raise the notion that this technique should

not be used in all high-risk patients with large aneurysms. However, the definitions used for high risk in EVAR trial 2 remain somewhat elusive. Guidelines for determining patient enrollment in EVAR trial 2 have been published;[21] however, "physician discretion" was also used in determining which patients were ultimately eligible for this trial. The insights provided by EVAR 2 are important. There is most certainly a population of patients with large aneurysms that are better treated medically than with surgical intervention. However, questions still remain about the risk factors that predict mortality in patients undergoing EVAR and the size of the population of patients that are truly high risk.

Sicard et al retrospectively analyzed data from five multi-center EVAR clinical trials to further characterize outcomes after EVAR.[22] These authors reported a 30-day mortality of 2.9% in a population of 565 patients that they defined as high risk, based upon criteria derived from EVAR trial 2 that included one or more of the following comorbidities: severe valvular disease, significant arrhythmia, uncontrolled CHF, dyspnea with stair climbing, poor pulmonary function, hypoxemia, hypercarbnia, or a serum creatinine $>$ 2.27mg/dL.[21] The mortality observed by Sicard et al was dramatically less than that found in EVAR 2 (2% versus 9%). Although there are several possible explanations for the dramatic difference in findings of the two studies, the most likely is that the "high risk" population defined by Sicard is indeed different than the high-risk cohort studied in EVAR trial 2. Patients recruited into clinical trials are usually homogeneous and patients with poor longevity or those at extremely high risk are often excluded from pivotal investigations. There are also exclusion criteria in clinical trials that eliminate patients with unfavorable arterial anatomy. It has previously been demonstrated that endovascular repair in patients with favorable anatomy is less risky. Despite apparent differences in mortality outcomes in these two studies, one can conclude from both that there is indeed a cohort of patients who are high risk for EVAR.

Our analysis further addresses this issue by providing information about the factors that define patients at high risk for EVAR. As well, we have provided insight into the size of the cohort that has a prohibitively high mortality. Of the almost 67,000 patients evaluated in this study, a risk of perioperative mortality of 9% or greater (the EVAR2 outcome) was found in only 1.3% of the treated population. We have also identified preoperative characteristics that can determine this small but high-risk cohort. We found that renal failure, lower extremity vascular disease, liver disease, neurological disorders, female gender, age, hospital volume, surgeon experience, heart failure, and chronic pulmonary diseases all increased the potential of death within 30 days following EVAR.

Multiple similar analyses have been performed for patients undergoing open aneurysm repair.[7-10] Although the demographic factors and comorbidities that increase mortality are similar for open and endovascular repair, their relative importance appears to differ. For EVAR, we found risk factors in descending order of importance to be: renal failure with dialysis, lower extremity ischemia, age $\geq$85 years, liver disease, CHF, renal failure without dialysis, female gender, a neurological disorder, chronic obstructive pulmonary disease, and low hospital volume and surgeon experience with EVAR. For open repair, renal failure leads the list (similar to EVAR), but is followed by myocardial disorders, such as ischemia and CHF, then pulmonary disease, age, and female gender.[10] One might predict that major heart and/or lung disease is of less relevance as a risk factor for endovascular aneurysm repair versus open repair and this appears to be the case. Perhaps it is not surprising that CHF or pulmonary disease are less important predictors of death in EVAR since the surgical intervention (groin cut-downs) is associated with a less profound physiologic demand on the heart and lungs.[23] In fact, the factors that lead to mortality following EVAR may be related more to complex arterial anatomy than to complex patient physiology.

Our multivariate analysis revealed that patients at highest risk are those with renal failure. Findings from the EUROSTAR registry were similar.[24] The increase in mortality associated with renal disease is possibly due to the high prevalence of multifocal atherosclerosis in these patients, including the heart and cerebrovascular circulation. Also of great significance is the strong association between renal failure and calcified and diseased iliac arteries.[25,26] When performing an EVAR in a patient with renal failure, the interventionalist may be faced with heavily calcified, tortuous, and narrowed iliac arteries that are difficult to navigate with an endovascular device. The consequence can be arterial rupture, occlusion, and the need for a conduit or a prolonged intervention. Thus, renal failure may be a surrogate for complex arterial anatomy. Unfortunately, one of the limitations of large datasets, such as Medicare, is the absence of information about anatomy; therefore, we are unable to verify this hypothesis.

A number of additional risk factors predicted perioperative mortality. Patients with lower extremity vascular disease are at increased risk presumably for the same reason as those with renal failure. Lower extremity vascular disease is also a marker for generalized atherosclerosis, including myocardial insufficiency. Patients with chronic liver disease experience greater morbidity and mortality following most elective surgeries.[27] In two small prospective studies, the influence of gender on outcome of EVAR was evaluated and no differences were found between men and women with respect to 30-day mortality.[28,29] In both studies, however, it was noted that women have a significantly higher rate of aborted procedures, less deployment success, and an increased risk of access-related complications. The lack of an association between gender and mortality in these smaller studies may be due to the small sample size, (n = 26)[29] and (n = 24).[28] The increased mortality that we observed in women may be largely related to anatomic issues. Anatomical characteristics inherent to women include shorter infrarenal necks, smaller proximal neck diameters, and smaller diameters of iliac (access) arteries.[29]

Neurological disorders, including a prior history of cerebrovascular accident and transient ischemic attack,

were present in 11.2% of our cohort, and were found to increase 30-day mortality by 59% in our multivariable regression model. Cerebrovascular disease has been observed to increase peri-procedural complications and mortality, and has, therefore, been included in several preoperative scoring systems, including the Revised Cardiac Risk Index,[30] Glasgow aneurysm score,[31] and the Customized Probability Model.[32] Additionally, we found surgeons just beginning their EVAR practice, as well as hospitals with lower annual volumes of EVARs, to have significantly higher perioperative mortality. We are not able to determine if surgeons at the early phase of their experience with EVAR are in mentored situations such as a group practice or an academic medical center. Possibly this might explain the low number of procedures necessary to gain expertise. Such volume-outcome relationships have long been recognized for open aneurysm repair[33] and it should be noted that despite the same opportunity for mentoring with open repair, the number of procedures necessary to achieve proficiency is significantly higher than for endovascular repair. We have composed a scoring system that can be used to assist interventionalists and patients. Assessing the surgical risk of a patient with multiple comorbidities can be remarkably difficult, yet it is these particular patients who benefit most from an accurate preoperative evaluation, as they are likely to have increased early and late mortality as a consequence of their associated illness. Preoperative risk stratification for noncardiac vascular surgery has been investigated by others and validated, using mathematical models to derive scoring systems and predict mortality.[10,30-32,35-37] Analysis of a large Medicare dataset provides sufficient statistical power to accurately identify specific individual criteria predictive of 30-day mortality for EVAR. Our scoring system allows a comparison of the impact of individual factors on mortality, and importantly, a summation of their combined effects. It is our hope that this scoring system can be used by the practicing interventionalist to identify those who are indeed candidates for EVAR. For example, a patient with CHF and chronic pulmonary disease would be at relatively low risk for repair (total score of four). Alternatively, a female patient with renal failure would be of profoundly high risk (total score of nine). We realize that scoring systems have their limitations, and in the real world clinicians need to individualize therapeutic decisions for patients. However, the scoring system that we have devised does take into account the majority of pertinent risk factors and could potentially be used as a guide to assist clinicians in their evaluation of patients with aneurysmal disease. Admittedly, our scoring system does not directly assess the important effect that vascular anatomy may have on outcome.

Other risk stratification systems have been employed to predict outcome of endovascular aneurysm repair.[34,35] Patients included in a randomized trial such as Dutch Randomized Endovascular Aneurysm Management (DREAM)[36] are selected and often more homogenous than those treated in standard practice. For example, many of the very-high-risk patients that are included in the Medicare database would not have passed screening criteria for a randomized trial. Moreover, in this analysis we have created a de novo scoring system from the data available rather than attempting to retrofit a scoring system previously designed for open repair for EVAR. That said, this is one of several proposed methodologies for risk-stratifying patients proposed for EVAR, and only future studies on new cohorts of patients will determine which of these systems has the greatest validity.

There are a number of limitations of administrative datasets that should be noted. First, knowledge of the severity of comorbidities is often lacking. Second, diagnosis codes are broad and vague and provide limited detail about the specific patient disease state. By accepting only comorbidities that are coded as chronic or that have been present on previous admissions, we may miss occasional comorbidites that have appeared between hospitalizations or that are not associated with a "chronic" code. By assuming this approach, we have likely increased our accuracy but may have also, to some extent, diminished our sensitivity. This is a common approach that is used in the evaluation of administrative data bases and overall the trade-off of accuracy for sensitivity is thought to be desirable. The third limitation, and possibly the most important for this analysis, is the lack of information regarding patient anatomy. We are not able to understand which of these 66,943 patients had diseased iliac arteries, nor do we know the size of the aneurysms treated. Lastly, as with all administrative datasets, there is the potential for coding inaccuracies and oversights. The effect of coding issues are likely diminished by the "randomization" of non-systematic errors that results when massive numbers of observations are statistically analyzed.[37] These limitations aside, the distinct advantage of administrative data bases such as Medicare, is the very large sample size. Our report of almost 67,000 EVARs is one of the largest ever published. This population-based dataset is rich in information regarding diagnoses, procedures, and demographics and is a true representation of clinical practice in the United States.

We determine high-risk EVAR patients by using a cohort of patients who have already undergone EVAR. This approach is frequently used to support clinician decision making on patient eligibility for various surgical procedures, including open repair of AAA.[7,9] However, it is important to note that clinical judgments made before patients receive EVAR may involved a different weighting of factors and may also take into account additional parameters versus those considered in this study. Our study stratifies operative risk only for patients already selected for EVAR. In the absence of compelling level I evidence (a randomized clinical trial of intervention versus no intervention), a retrospective analysis of surgical outcomes has proven to be a useful approach for operative risk stratification.

It should be noted that multiple studies have supported a considerably high incidence of death from rupture in high-risk AAA cohorts that are treated conservatively.[21,38,39] Thus, a significant portion of the AAA population will likely die from rupture if they are excluded

from endovascular repair. Our data reveal the existence of a subgroup of patients who are indeed high risk for endovascular repair. However, we also show that this cohort of patients is exceedingly small. In sum, we believe that EVAR is safe and effective in the majority of the elderly population, even those with multiple comorbidities. The proportion of patients truly unfit for EVAR is small. Moreover, we feel that the described scoring system can be a useful aid to preoperatively identify patients unfit for even minimally invasive treatment of their aneurysm.

AUTHOR CONTRIBUTIONS

Conception and design: NE, JG, AG, CK
Analysis and interpretation: NE, JG, GG, AG, AM, JM, CK
Data collection: NE
Writing the article: NE, JG, CK
Critical revision of the article: NE, JG, GG, AG, AM, JM, CK
Final approval of the article: NE, JG, GG, AG, AM, JM, CK
Statistical analysis: NE
Obtained funding: AG, AM, CK
Overall responsibility: NE

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INVITED COMMENTARY

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Predictive assessment of mortality and morbidity remains an important component of preoperative evaluation of any surgical procedure. Most preoperative risk assessment models have been developed for open surgical procedures with variable predictability.[1,2] The introduction and widespread use of less invasive surgical procedures, either by laparoscopic or endovascular techniques has heightened the need for developing new risk models that could predict postoperative mortality and morbidity.

Treatment of abdominal aortic aneurysm has undergone dramatic changes in the last two decades. Despite the many advances in anesthetic management, preoperative risk factor modifications, and postoperative care, the 30-day mortality has remained between 3% and 5% with higher mortality and morbidity in high-risk patients.[3] Despite the significant threefold reduction in mortality in single centers, statewide databases and randomized trials, compared with conventional open repair, no analysis of criteria has been performed that can objectively identify those risk factors that increase 30-day mortality in endovascular aneurysm repair (EVAR). The EVAR 2 trial used a series of medical risk factors and "pragmatic" approaches to deem a patient unsuitable for AAA repair.[4] Our group reported much lower 30-day mortality (2.9% vs 9%) for high-risk patients compared with EVAR 2 trial based on medical comorbidities.[5] Both reports were based on risk factors commonly used to predict mortality in open repair not specific to EVAR.

In this issue, Drs Egorova, Giacovelli, and collaborators describe an extensive analysis of the Inpatient Medicare database of patients with elective abdominal aortic aneurysm (AAA) repair from 2000 to 2006 and develop a risk model of preoperative 30-day mortality in over 66,000 patients treated by EVAR. Although some of the preoperative comorbidities that predict higher 30-day mortality are similar to those described for open repair, some factors are different and other similar factors have a different predictor effect on 30-day outcomes. This preoperative score, as a predictor of 30-day mortality, provides for the first time, an objective indicator of the mortality risk specific for EVAR in high-risk patients. Another important observation of this report is the identification of a very small number of EVAR candidates that are truly very high-risk even for this less invasive procedure. This preoperative predictive score will be of great utility to interventionalists who frequently perform EVAR.

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Appendix (online only). List of ICD-9-CM codes for comorbidities

Comorbidity	*ICD9 code*
	Index hospitalization
Congestive heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.91, 404.13, 404.93, 425.4, 425.5, 425.7, 425.8, 425.9, 428.0, 428.1, 428.20, 428.22, 428.30, 428.32, 428.40, 428.42, 428.9
Cardiac arrhythmia	426.0, 426.10, 426.11, 426.12, 426.13, 426.7, 426.9, 427.0, 427.1, 427.2, 427.3, 427.9, V45.0, V53.3
Valvular disease	093.2, 394, 395, 396, 397, 424, V42.2, V43.3
Coronary disease	412, 413, 414, 429.2
Diabetes	250
Hypertension	401, 402, 403, 404, 405
Pulmonary diseases	416, 417.9, 490, 491, 492, 493, 494, 495.0, 495.1, 495.2, 495.3, 495.4, 495.5, 495.6, 495.8, 495.9, 496, 500, 501, 502, 503, 504, 505, 506.0, 506.2, 506.4, 506.9, 508.1, 508.8, 508.9
Clinically significant lower extremity vascular diseases	440.22, 440.23, 440.24, 440.3, 444.22, V43.4,
Renal atherosclerosis	440.1
Vascular intestine disease	557.1
Renal failure with dialysis	V45.1, V56.0, V56.1, V56.2, V56.3, V56.8, 585.6, 39.95 (w/o 586)
Renal failure without dialysis	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585 (w/o 585.6), 588.0
Other renal diseases	582, 583.0, 583.1, 583.2, 583.4
Kidney transplant	V420
Liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.9, 456.0, 456.1, 571, 572.1, 572.2, 572.3, 572.4, 572.8, 573.0, 573.1, 573.8, 573.9
Cerebrovascular diseases and paralysis	342, 344.1, 344.3, 344.4, 344.5, 344.9, 437.0, 438
Other neurological diseases	330, 331, 332, 333, 334.0, 334.1, 334.2, 334.4, 334.8, 335.0, 335.1, 335.2, 335.8, 335.9, 336.0, 336.2, 343, 344.0, 348.1, 348.3, 344.2, 344.6, 345, 437.3, 437.4, 437.5, 437.6, 437.7
Cancer	140, 141, 142, 143, 144,145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158,159, 160, 161, 162, 163, 164, 165, 170, 171,172, 174, 175, 176, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203.0, 238.6
Rheumatoid arthritis	446, 701.0, 710.0, 710.1, 710.2, 710.3, 710.4, 710.8, 710.9, 711.2, 719.3, 714, 720, 725, 728.5, 728.89
	Pre-index hospitalizations
History of heart failure	398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.91, 404.13, 404.93, 425.4, 425.5, 425.7, 425.8, 425.9, 428
Cardiac arrhythmia	426, 427.0, 427.1, 427.2, 427.3, 427.4, 427.5, 785.0, 996.01, 996.04, V45.0, V53.3
Valvular disease	093.2, 394, 395, 396, 397, 424, V42.2, V43.3
Coronary disease	410, 412, 413, 414, 429.2
Pulmonary	415, 416, 417, 490, 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 506.0, 506.2, 506.4, 506.9, 508
Clinically significant lower extremity vascular diseases	440.22, 440.23, 440.24, 440.3, 444.22, 996.7, V43.4
Renal atherosclerosis	440.1, 445.81
Vascular intestine disease	557.1, 557.9
Hypertension	401, 402, 403, 404, 405, 458.0, 458.1, 458.8, 458.9
Cerebrovascular diseases and paralysis	342, 344.1, 344.3, 344.4, 344.5, 344.9, 362.30, 362.31, 362.34, , 433, 434, 435, 436, 437.8, 437.9, 438, 784.3
Other neurological diseases	330, 331, 332, 333, 334.0, 334.1, 334.2, 334.3, 334.4, 334.8, 334.9, 336.0, 335.0, 335.1, 335.2, 335.8, 335.9, 336.0, 336.2, 340, 343, 344.0, 344.2, 344.6, 345, 348.1, 348.3, 430, 431, 432, 437.3, 437.4, 437.5, 437.6, 437.7, 780.3
Diabetes	250
Dialysis	V45.1, V56.0, V56.1, V56.2, V56.3, V56.8, 585.6, 39.95
Renal failure without dialysis	403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 585 (w/o 585.6), 586, 588.0
Renal diseases	582, 583.0, 583.1, 583.2, 583.4, 583.6, 583.7
Liver disease	070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9,456.0, 456.1, 456.2, 571, 572.2, 572.3, 572.4, 572.8, 573
Cancer	140, 141, 142, 143, 144,145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158,159, 160, 161, 162, 163, 164, 165, 170, 171,172, 174, 175, 176, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203.0, 238.6
Kidney transplant	V42.0
Rheumatoid arthritis	446, 701.0, 710.0, 710.1, 710.2, 710.3, 710.4, 710.8, 710.9, 711.2, 719.3, 714, 720, 725, 728.5, 728.89, 729.30